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b) a container comprising at least one bifunctional linker molecule, which has a first portion specific for one of said oligonucleotide anchors and a second portion that comprises a probe which is specific for a nuclease protection fragment which is specific for one of said nucleic acids, and

c) one or more nucleases effective for digesting single strand nucleic acid and/or the RNA strand of a DNA/RNA duplex.

56. A kit useful for the detection of at least one nucleic acid target in a sample, comprising

a) a surface, comprising multiple spatially discrete regions, at least two of which are substantially identical, each region comprising at least two different oligonucleotide anchors, and

b) a set of instructions for i) performing a nuclease protection procedure on said nucleic acid(s) of interest, using a nuclease protection fragment(s) specific for said nucleic acid(s), and ii) attaching to at least one of said oligonucleotide anchors a bifunctional linker molecule, which has a first portion specific for at least one of said oligonucleotide anchors and a second portion that comprises a probe which is specific for at least one of said nuclease protection fragments.

Concluded --

REMARKS

The Claims

The above amendments and newly added claims are drawn to methods and kits which, among other things, involve contacting a sample with a nuclease protection fragment specific for a target and with a nuclease, and then contacting the resultant sample with the recited combination, thereby binding to the latter any nuclease protection fragment(s) (*i.e.*, subjecting the target sample to a nuclease *before* contacting it with said combination, as opposed, *e.g.*, to the procedures of USP 5,770,370, of record) (see, *e.g.*, amended claim 15).

Many of the new claims now recite the number of anchors as being, *e.g.*, at least 2, rather than at least 8, as before. This recitation is supported, *e.g.*, in the specification at page 11, line 14.

The new claims recite specific embodiments of the invention and are fully supported in the specification. For example, recitations involving nuclease protection reactions are supported, *e.g.*, at page 35, line 20 to page 38, line 13. New claim 29 is supported in the specification, *e.g.* at page 17, lines 6-8. The limitations in claims 49 and 50 that at least one of the targets is a DNA molecule and at least one an RNA molecule, or that at least one of the

nuclease protection fragments is specific for a DNA molecule and at least one for an RNA molecule, are supported, *e.g.*, in the specification at page 6, lines 12-14. The recitation in new kit claim 53 that the nuclease protection fragment in the kit is specific for a nucleic acid of interest, but not for any of the oligonucleotide anchors in said kit, is supported, *e.g.*, at page 36, lines 10-13.

These claims are essentially the same as those pending in U.S. Ser. No. 09/109,076.

With regard to the outstanding rejections in the parental case, U.S. Ser. No. 09/218,166:

The Abstract

The Abstract (on a separate page) has been amended to be one paragraph rather than two.

Rejections under 35 U.S.C. § 112, second paragraph

The terms which the Examiner alleges to be indefinite are fully described in the specification and need not be amended. Taken in the order in the office action:

1) The nature of the "association" of anchors and linkers is described, *e.g.*, at page 10, lines 11-14:

> As used herein, an "anchor/linker complex" exists when an anchor and a linker have combined through molecular *association* in a specific manner. [emphasis added]. The interaction with the linker can be either irreversible, such as via certain covalent bonds, or reversible, such as via nucleic acid hybridization.

2) "Substantially identical" regions are described, *e.g.*, at page 8, line 28 to page 9, line 6:

> Substantially identical regions, as used herein, refers to regions which contain identical or substantially identical arrays of anchors and/or anchor/linker complexes. Substantially identical, as used herein, means that an array or region is intended to serve essentially the same function as another array or region in the context of analyzing a target in accordance with this invention. Differences not essentially affecting function, *i.e.*, detectability of targets, are along the line of small nucleotide imperfections (omissions/inserts/substitutions) or oligo imperfections (poor surface binding), etc., which do not within assay accuracy significantly affect target determination results.

3) Applicants do not understand the rejection over the word "portion." In claim 11,

part c), it is clear that a bifunctional linker contains two portions, each having a different specificity.

The statutory double patenting rejection; the non-statutory double patenting rejection; and the rejections under 35 U.S.C. § 103

Claims 11-14 have been canceled. Therefore, the above rejections are moot.

In a related PCT application (PCT/US 98/27191), two references were cited as X references with regard to the instantly claimed invention: WO97/31256 and Niemeyer *et al.* (1994), both of which are already of record in the instant application. For the WO, see the IDS of Dec. 2, 1999. For Niemeyer, see the IDS of Dec. 22, 1998, last sentence, where attention was drawn to it and, *i.a.*, to USP 5,545,531 (Rava *et al.*). Three co-pending applications related to the present one have received first office actions on the merits: 09/109,076 (filed 7/2/98), 09/218,089 (filed 12/22/98) and 09/337,325 (filed 6/21/99). References relied upon in these office actions include, in addition to some of those discussed above, USP 5,770,370 (Kumar), which is of record in the instant application. See the IDS of Dec. 22, 1998. Two other references were cited and/or relied upon in, *e.g.*, 09/218,089. These references, Pease *et al.* (1994). *Proc. Natl. Acad. Sci. USA* 91, 5022-5026 and USP 5,445,934 (Fodor *et al.*) are believed to be cumulative and were filed in an IDS dated July 14, 2000.

USP 6,083,763 (submitted in the accompanying IDS), which relates to aspects of the prior claims, does not disclose or suggest a method in which nuclease protection is involved.

Respectfully submitted,

Anthony J. Zelano (Reg. No. 27,969)
Attorneys for Applicants
Nancy J. Axelrod (Reg. No. 44,014)
Patent Agent

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza I
2200 Clarendon Boulevard, Suite 1400
Arlington, Virginia 22201
(703) 812-5304 [Direct Dial]
E-mail address: axelrod@mwzb.com

Filed: **September 15, 2000**

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